F. PHYSICAL CHEMICAL DESCRIPTION

Hexamethoxymethylmelamine cannot be synthesized as a pure product. Instead, it is formed as a mixture with methylated melamine-formaldehyde polymer. The data for all physical and chemical properties shown below are estimated by EPIWIN based on 100% HMMM.

1. MELTING POINT

Test substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the MPBPWIN Program (v.1.40)[1], using the adapted Joback and Gold and Ogle Methods. Weighted value for melting point.
GLP:	Not applicable to estimations
Year:	2002
Results:	188.40 °C
Remarks:	The melting point calculation by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch *et al*. (1997)[2].
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

2. BOILING POINT

Test substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the MPBPWIN Program (v.1.40)[1], using the adapted Stein and Brown Method.
GLP:	Not applicable to estimations
Year:	2002
Results:	448.20 °C
Remarks:	The boiling point calculation by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch *et al*. (1997)[2].
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p.52.

3. VAPOR PRESSURE

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the MPBPWIN Program (v.1.40)[1], using the Modified Grain Method.
GLP:	Not applicable to estimations
Year:	2002
Results:	1.06×10^{-8} mmHg @ 25 °C
Remark:	The vapor pressure calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch *et al.* (1997)[2].
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p.52.

4. PARTITION COEFFICIENT

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the KowWin Program (v.1.66)[1]
GLP:	Not applicable to estimations
Year:	2002
Results:	Log K_{ow} = 1.61
Remark:	The partition coefficient calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997)[2].
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p.52

5. WATER SOLUBILITY

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated from K_{ow} with WSKOW (v1.40)[1] : KowWin Estimate
GLP:	Not applicable to estimations
Year:	2002
Results:	149.3 mg/L @ 25°C
Remark:	The water solubility calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p.52.

G. ENVIRONMENTAL FATE DATA

1. PHOTODEGRADATION

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the AOP program (v1.90)[1], which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	Not applicable to estimations
Year:	2002
Results:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is relatively rapid. Rate constant: 323.5521 x 10^{-12} cm^3/molecule-sec Half-life: 23.802 minutes
Remark:	The photodegradation rate calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p.52.

2. HYDROLYSIS

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by the HYDROWIN program (v1.67)[1].
GLP:	Not applicable to estimations
Year:	2002
Results:	No estimate available.
Remark:	No data on HMMM as an independent material is available, nor can HMMM be tested as an independent material. HMMM is formed as a reaction product in addition to several other reaction products when melamine crystal is methylolated and methylated. As such, HMMM cannot be tested for hydrolysis potential.
Reference:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000.

3. TRANSPORT (FUGACITY)

Test Substance: Hexamethoxymethylmelamine, CAS # 3089-11-0

Method: Estimated by the Level III Fugacity Model (Full-Output)

GLP: Not applicable to estimations

Year: 2002

Results: MacKay Level III Fugacity Model

Medium	Concentration %	Emissions (kg/hr)
Air	6.45e-5	1000
Water	36.1	1000
Soil	63.8	1000
Sediment	0.0996	0

Medium	Concentration %	Emissions (kg/hr)
Air	5.43e-5	1000
Water	25.9	0
Soil	74	0
Sediment	0.0715	0

Medium	Concentration %	Emissions (kg/hr)
Air	3.28e-12	0
Water	99.7	1000
Soil	4.68-6	0
Sediment	0.275	0

Medium	Concentration %	Emissions (kg/hr)
Air	3.61e-10	0
Water	23	0
Soil	76.9	1000
Sediment	0.0635	0

Remark: The fugacity calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]

References: [1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

4. BIODEGRADATION

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by STP Fugacity Model: Predicted Fate in a Wastewater Treatment Facility and by BIOWIN (v.4.000).[1]
GLP:	Not applicable to estimations
Year:	2002
Results:	Linear Model Prediction: Does not biodegrade fast Non-linear Model Prediction: Does not biodegrade fast Ultimate Biodegradation Timeframe: Recalcitrant Primary Degradation Timeframe: Weeks-Months MITI Linear Model Prediction: Does not biodegrade fast MITI Non-Linear Model Prediction: Does not biodegrade fast The material is not predicted to be readily biodegradable, but is predicted to be inherently biodegradable.
Remark:	The biodegradation rate calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]
References:	[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000. [2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

H. ECOTOXICITY DATA

1a. ACUTE TOXICITY TO FISH[1]

Test Substance:	~34-44% Hexamethoxymethylmelamine, CAS # 3089-11-0; 38-40% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	OECD Guideline 203
Type:	static
Species:	Bluegill Sunfish (Lepomis macrochirus (Fish, fresh water))
Exposure period:	96 hour(s)
Analytical monitoring:	Exposures based on nominal concentrations
Year:	1993
GLP:	This test was conducted in general agreement with GLP regulations and was performed to comply with OECD GLP regulations.
Results:	LC50 = > 603.1 mg/L; None of the fish in at any test concentration died by 96 hours.
Remark:	This study is assigned a reliability code of 2b according to the criteria established by Klimisch *et al.* (1997)[2].

Summary details:
An initial range finding test was performed to determine the optimal concentrations for the test. This 96-hour static, non-renewal bioassay was performed on six (6) groups of 10 bluegill sunfish approximately 29 weeks of age at initiation of exposure . The fish were housed (10 per tank) in 8.5L glass tanks containing 3.6L of laboratory dilution water (Blend Water 2). The treatment concentrations were: 1.0, 0.5, 0.25, 0.12, 0.06 g/L and a laboratory dilution water control (BW2). Tests were performed in duplicate. Individual treatments were prepared by adding the appropriate amount of test material to laboratory dilution water which was stirred for 1 hour and 20 minutes until treatment solutions appeared clear. Water hardness of the dilution water ranged between 72 and 84 mg/L, as $CaCO_3$. Fish were maintained at 22.3°C (22.0-22.9) under a 16hr/8hr light/dark cycle. Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The pH values were 7.0-7.6. Dissolved oxygen levels ranged from 8.4 (on day 0) – 6.5 (on day 4), the dissolved oxygen values on day 3 dropped below 60% of saturation in some of the chambers. Aeration with glass pipettes was initiated in all test chambers for the remainder of the study. The LC50 was determined based on the Water Accommodated Fraction (WAF) of each solution for a period of 96 hours. No test material

insolubility or feces were noted in any replicate chambers. Observations for mortality, abnormal behavior and appearance of the fish were performed on all replicate chambers at 24, 48, 72 and 966 hours. No mortality occurred during the 96-hour period.

References: [1]Exxon Biomedical Sciences, Inc. Project Number: 142940, Fish, Acute Toxicity Test, Conducted for Cytec Industries Inc., May 7, 1993

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1b. ACUTE TOXICITY TO FISH[1]

Test Substance:	~28±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~72% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009
Type:	static
Species:	Bluegill Sunfish (Lepomis macrochirus (Fish, fresh water))
Exposure period:	96 hour(s)
Analytical monitoring:	Exposures based on nominal concentrations
Solvent:	Acetone
Year:	1984
GLP:	Yes
Results:	LC50 = > 1,000 mg/L; NOEC 350 mg/L None of the fish in at any test concentration died by 96 hours, abnormal effects of surfacing, dark discoloration and/or fish on bottom were observed in the 560 and 1,000 mg/L test concentrations.
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch *et al.* (1997)[2]. Meets generally accepted scientific standards and is described in sufficient detail

Summary details:
An initial range finding test was performed to determine the optimal concentrations for the test. The preliminary test concentration was set at 100 mg/l. From this information, five concentrations of the test compound with 10 fish per beaker were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/L and included a dilution water control and solvent control. The total hardness of the dilution water was 40-45 mg/L, as $CaCO_3$. The solvent control received an aliquot (7.5 ml) of acetone, equivalent to that used in preparation of all test concentrations. A reference material, Anitmycin A was used as a challenge to verify that the fish were in good condition.

The fish were added to the test chambers by random assignment within 30 minute after the addition of test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects such as surfacing, loss of equilibrium and dark discoloration. Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The dissolved oxygen concentrations, which ranged from 7.4 to 9.7 mg/L, representing 84 and 110% saturation at 22C, were adequate. The pH values ranged from 7.0 to 7.2. The test vessels were kept in a water bath at a constant 22C.

The LC50 was determined from the nominal concentrations of 100, 180, 320, 560, and 1,000 mg/L. The 96-Hr LC50 for Antimycin A was 1.2 E-4 mg/L. The NOEC for the test material was 320 mg/L. No mortality occurred during the 96-hour period.

References:

[1]ABC Laboratories, Inc. Columbia, MO. Acute Toxicity of Resimene® 745 to Bluegill Sunfish, Report # 31224. Conducted for Monsanto Company, January 27, 1984.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1c. ACUTE TOXICITY TO FISH[1]

Test Substance: ~28±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~72% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0

Method: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009

Type: static

Species: Rainbow Trout (Salmo gairdneri)

Exposure period:	96 hour(s)
Analytical monitoring:	Exposures based on nominal concentrations
Solvent:	Acetone
Year:	1983
GLP:	Yes
Results:	LC50 = > 1,000 mg/L; NOEC 560 mg/L None of the fish in at any test concentration died by 96 hours, abnormal effects of surfacing and fish on the bottom were observed in the 1,000 mg/L test concentrations.
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch *et al.* (1997)[2]. Meets generally accepted scientific standards and is described in sufficient detail

Summary details:
An initial range finding test was performed to determine the optimal concentrations for the test. The preliminary test concentrations were set at 0.1, 1.0, and 100 mg/l. From this information, five concentrations of the test compound with 10 fish per beaker were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/L and included a dilution water control and solvent control. The total hardness of the dilution water was 40-45 mg/L, as $CaCO_3$. The solvent control received an aliquot (7.5 ml) of acetone, equivalent to that used in the preparation of all test concentrations. A reference material, Anitmycin A was used as a challenge to verify that the fish were in good condition.

The fish were added to the test chambers by random assignment within 30 minute after the addition of test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects such as surfacing, loss of equilibrium and dark discoloration. Water quality measurements (pH, dissolved oxygen, and temperature) were performed daily on each chamber. The dissolved oxygen concentrations, which ranged from 7.6 to 9.5 mg/L, representing 70 and 88% saturation at 12C, were adequate. The pH values ranged from 7.0 to 7.6. The test vessels were kept in a water bath at a constant 12C.

The LC50 was determined from the nominal concentrations of 100, 180, 320, 560, and 1,000 mg/L. The 96-Hr LC50 for Antimycin A was 2.9 E-5 mg/L. The NOEC for the test material was 560 mg/L. No mortality occurred during the 96-hour period.

References:

[1]ABC Laboratories, Inc. Columbia, MO. Acute Toxicity of Resimene® 745 to Rainbow Trout, Report # 31225. Conducted for Monsanto Company, December 22, 1983.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and

ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1d. ACUTE TOXICITY TO FISH

Test Substance:	Hexamethoxymethylmelamine, CAS # 3089-11-0
Method:	Estimated by ECOSAR using triazines as the reference material.[1]
Species:	Freshwater Fish
Exposure period:	96 hour(s);14-day
Year:	2002
GLP:	Not applicable to estimated values
Results:	96 Hour LC50 = 673.22 mg/L 14-day LC50 = 1146.17 mg/L
Remark:	This study is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997)[2]. This estimated value is similar to that obtained experimentally for bluegill sunfish.
Other Information:	**48-hour LC50 (Orange-red killifish) = 680 mg/L**. 48-hour semi static test on Orange-red killifish (*Oryzias latipes*); Data reported on CITI (Chemical Inspection and Testing Institute) Web site.
Remark:	This study is assigned a reliability codes of 4d and 4e according to the criteria established by Klimisch *et al.* (1997)[2].

References:

[1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

2a. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test substance:	~28±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~72% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975). EPA Guideline 660/3-75-009
Species:	Daphnia magna
Exposure period:	48 h
Test Concentrations:	Daphnia were exposed to concentrations of 100, 180, 320, 560 and 1,000 mg/L.
Vehicle:	Acetone
Analytical monitoring:	No; Testing based on nominal concentrations.
GLP:	Yes.
Year:	1983
Results:	LC_{50} > 1000 mg/L NOEC = 320 mg/L (based on the lack of mortality and abnormal effects). Although no mortality was observed in the test concentrations of 100-1,000 mg/L, abnormal effects of surfacing and daphnids lying on the bottom of the test chambers were observed in the 1,000 and 560 mg/L test concentrations.
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch *et al.* (1997)[2]. Meets generally accepted scientific standards and is described in sufficient detail

Summary details:

The static daphnia bioassay was conducted in 250 ml glass beakers containing 200 ml of ABC well water (total hardness 255 ppm, as $CaCO_3$). These vessels were kept at 20 (2C) in a temperature controlled area. The lighting was maintained at 50-70 foot candles on a 16 hour daylight photoperiod. Dissolved oxygen concentrations ranged between 8.0 and 8.1 mg/L representing 87 and 88 percent saturation at 20C, respectively. The pH values of the treated chambers were consistent with the control and ranged from 8.2 to 8.7.

An initial range finding experiment was conducted using 5 Daphnia each in exposure concentrations of 1.0, 10, and 100 mg/l. From this information, five concentrations in duplicate of the test compound with 10 Daphnia per beaker were selected for the definitive bioassay. These concentrations were a logarithmic series ranging from 100 to 1,000 mg/L and included a control and solvent control. The solvent control received an aliquot of 1.0 ml of acetone, equivalent to that of the highest test concentration. All concentrations were observed once every 24 hours for mortality and abnormal effects such as surfacing, clumping of the Daphnia and Daphnids lying on the bottom of the test chambers.

Reference: [1]Acute Toxicity of Resimene® 745 to *Daphnia magna*; ABC Laboratories, Inc., Columbia, Missouri; Final Report # 31226.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

2b. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance: Hexamethoxymethylmelamine, CAS # 3089-11-0

Method: Estimated by ECOSAR using triazines as the reference material.[1]

Species: Daphnia magna

Exposure period: 48 hour(s);16-day

Year: 2001

GLP: Not applicable to estimated values

Results: 48 Hour EC50 = 702.2 mg/L
16-day EC50 = 30.4 mg/L

Remark: This study is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997)[2].

References: [1]EPI Suite U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics and Syracuse Research Corporation, Syracuse, NY, 2000.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and

ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

3. TOXICITY TO AQUATIC PLANTS

Test Substance: Hexamethoxymethylmelamine, CAS # 3089-11-0

No data found.

I. MAMMALIAN TOXICITY

1a. ACUTE ORAL TOXICITY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Limit Test. OPPTS Guideline 870.110/OECD Guideline 401
Type:	oral LD50
Species/Strain:	rat/Sprague Dawley
Sex:	male/female
Number of animals:	10 (5/sex)
Vehicle:	None. Material administered as received.
Year:	2001
GLP:	Yes
Results:	LD50 = > 2000 mg/kg
Remark:	This study is assigned a reliability code of 1a according to the criteria established by Klimisch et al. (1997). GLP guideline study.

Summary details:

A limit test was performed in which one group of five male and five female rats received a single oral 2000 mg/kg dose of the test article. Following dosing, the animals were observed daily for clinical abnormalities and twice daily for health/mortality checks. The animals were weighed before dosing and then weekly. A gross necropsy was performed on all animals at the time of death or scheduled euthanasia.

The animals room temperature and relative humidity ranges were 18-23ºC and 40-76%, respectively. Room temperature and relative humidity were monitored daily. Food (except during fasting overnight prior to dosing) and water were provided ad libitum. Animals were randomly selected and subject to a detailed pretest observation prior to dosing. Only healthy animals were chosen for the study.

One out of 5 males and 3/5 females died during the study. All mortality occurred by study day 2. Clinical abnormalities observed during the study included prostration, breathing abnormalities, no feces, apparent hypothermia, dilated pupils, ocular discharge, eyelids partially closed and

decreased food consumption. Body weight gain was noted for all surviving animals during the test period. Gross internal observations for the animals that died included foci on the thymus, dark red lungs, blackish-purple spleen, abnormal content of the bladder, and abnormal content of the digestive system. No significant gross internal findings were observed at necropsy on study day 14.

References:

[1]An Acute Oral Toxicity Study in Rats with Resimene® 745, Springborn Laboratories, Inc. for Solutia, Inc. Study Report # 3463.98/SB200110015, November 12, 2001

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. See Listing of Codes, p. 52.

1b. ACUTE ORAL TOXICITY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Follows method described in FIFRA (November, 1982 Section 81-1) and in TSCA: Health Effects Test Guidelines, August 1982.
Type:	oral LD50 with range finder
Species/Strain:	rat
Sex:	male/female
Number of animals:	50
Vehicle:	Material dosed as received.
Year:	1984
GLP:	no
Results:	LD50 = 1800 mg/kg average (2000 mg/kg males) (1600 mg/kg females)
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch et al. (1997). Meets generally accepted scientific standards and is described in sufficient detail.

Summary details:

The animal room temperature and relative humidity ranges were 19.4-24.4ºC and 30-70%, respectively. Room temperature and relative humidity were monitored twice daily. Food (except during fasting overnight prior to dosing) and water were provided ad libitum. Animals were randomly selected and subject to a detailed pretest observation prior to dosing. Only healthy animals were chosen for the study.

Animals were dosed with the test article as received by oral intubation using a ball-tipped intubation needle fitted onto a syringe. Doses were calculated using fasted body weights.

Animals were checked for viability twice daily and were observed for clinical signs at 1, 2, and 4 hours post-dosing and then daily thereafter for 14 days. Body weights were determined pre-fast, just prior to dosing, and on days 7 and 14.

Range Finder: Ten (one/sex/dose level) animals received 50, 100, 500, 1000, or 2000 mg/kg. No post-mortem examinations were performed. Only 1 animal at the 2000 mg/kg dose level died on study. Based on this the doses for the LD50 study were selected.

LD50 Study: 10 (5/sex) animals per dose level received 625 mg/kg, 1250 mg/kg, 2500 mg/kg or 5000 mg/kg.

Mortalities were as follows:

Dose Level (mg/kg)	Males	Females	Total	Time to Death
625	0/5	0/5	0/10	-
1250	1/5	2/5	3/10	22 hrs
2500	5/5	5/5	10/10	2-47 hrs
5000	3/5	4/5	7/10	0-47 hrs

Gross postmortem examinations were performed on all animals which died or were found dead during the study. All animals surviving at termination of study on day 14 were killed and examined grossly. All abnormalities were recorded but no tissues were saved.

Clinical signs: Signs seen during the 24 hours after dosing inmost or all groups included ataxia, hypoactivity, prostration, hypopnea, wet rales and oral, nasal and ocular discharge. Other signs occurred sporadically. Animals which survived beyond 24 hours generally exhibited decreased food consumption and unthrifty coats for several days after dosing. However, all survivors were free of significant abnormalities by termination of the study (day 14).

Gross Postmortem Observations:
Examination of animals which died revealed a variety of changes, primarily in the lungs and gastrointestinal tract; most of these were considered to represent postmortem changes or to demonstrate the presence of the test material in the gastrointestinal tract. Reddening of the stomach and intestinal walls and the presence of red fluid in the stomach and intestines seen in

several animals may represent an irritant effect of the test material on gastrointestinal mucosa. Animals killed after 14 days exhibited changes similar to those seen in control animals.

References: [1]Acute Oral Toxicity Study in Rats, Bio/Dynamics Inc for Monsanto Company, Report # 4702-83/BD-83-268, August, 1984

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1c. ACUTE ORAL TOXICITY[1]

Test Substance: ~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0

Method: Single Oral Dose-Undiluted.

Type: oral LD50

Species/Strain: rat/Sprague-Dawley

Sex: male/female

Number of animals: 20

Vehicle: None

Year: 1976

GLP: no

Results: LD50 = 7,400 mg/kg

Remark: This study is assigned a reliability code of 2e according to the criteria established by Klimisch et al. (1997)[2]. Meets generally accepted scientific standards, well-documented and acceptable for assessment.

Summary details:

Animals were dosed as received with 5,010, 6,310, 7,940, or 10,000 mg/kg. Mortalities were as follows:

Dose Level (mg/kg)	Males	Females	Total	Time to Death
5010	1/3	0/2	1/5	1-3 days
6310	0/2	1/3	1/5	
7940	1/3	2/2	3/5	
10000	2/2	3/3	5/5	

Clinical signs: Clinical observations included reduced appetite and activity (2 to 4 days in survivors), increasing weakness, collapse, and death.

Gross Postmortem Observations: Gross autopsy showed hemorrhagic areas of the lungs and liver and acute gastrointestinal inflammations. In animals surviving to 14 days, viscera appeared normal.

References: [1]Acute Oral Toxicity, Monsanto Company, August, 1976.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1d. ACUTE ORAL TOXICITY[1]

Test Substance: ~50% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~50% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0

Method: Test material suspended in water. Animals dosed by oral gavage and observed over a 7-day period for physical condition and mortality.

Type: oral LD50

Species/Strain: rat

Sex: male

Number of animals: 10

Vehicle: water

Year: 1960

GLP: no

Results: LD50 = > 5 g/kg

Remark:	This study is assigned a reliability code of 3a according to the criteria established by Klimisch et al. (1997). Documentation insufficient for assessment, therefore this study is not considered valid.

Summary details:

The material ~50% HMMM was diluted with water to give a dispersion containing 0.2 g solids per ml which was administered orally to young male albino rats. Dosages of 5 g/kg and 10 g/kg produced mortalities of 0/5 and 4/5 during the following seven days. Consequently, the single oral dose LD50 is considered to be greater than 5.0 g/kg.

References: [1]Acute Oral Toxicity, American Cyanamid, December, 1960

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1e. ACUTE DERMAL TOXICITY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Acute Dermal LD50 Study
Type:	dermal LD50
Species/Strain:	rabbit/ New Zealand Whites
Sex:	male/female
Number of animals:	3
Vehicle:	none
Year:	1976
GLP:	no
Results:	LD50 = >7,940 mg/kg
Remark:	This study is assigned a reliability code of 2e according to the criteria established by Klimisch et al. (1997)[2]. Meets generally

accepted scientific standards, well-documented and acceptable for assessment.

Summary details:

A dose of 5,010 or 7,940 mg/kg was administered topically to the skin of 3 rabbits, 1 male at the low dose and 1/sex at the high dose. All animals were throughout the 14-day study. On day 14 surviving animals were humanely killed and gross postmortem examinations were performed.

No deaths occurred. Specific signs of toxicity observed included reduced appetite and activity (two to four days). Gross port-mortem examination revealed no significant findings related to treatment.

References:

[1]Acute Dermal Toxicity, Monsanto Company, August, 1976.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1f. PRIMARY EYE IRRITATION STUDY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Primary Eye Irritation Study according FHSA
Type:	Primary Eye Irritation
Species/Strain:	Rabbits/New Zealand Albino
Sex:	unknown
Number of animals:	6
Year:	1976
GLP:	no
Results:	Slight eye irritant
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch et al. (1997)[3]. Meets generally accepted scientific standards and is described in sufficient detail.

Summary details:

A single dose of 100 microliters of undiluted test material was placed in the cupped lower lid of the one of each rabbit; the untreated eye served as the control. The material was left in the eye for 24-hours.. During the 7 day study, the eyes were examined for discharge, chemosis, inflammation, and opacity at 10 minutes, 1 hour, 24 hours and on days 2, 3, 5, and 7 after dosing and Ocular Irritation Scores (Draize Scores) were calculated. All rabbits survived.

Ocular exposure produced immediate discomfort, considered moderate, with eyes tightly closed. At 10 minutes post exposure there was moderate erythema and copious discharge. At 1 hour there was slight to moderate erythema and copious discharge. At 24 ours there was slight erythema, copious discharge with slight whitish exudate. By 48 hours there was gradual improvement. By 72 hours there were no signs of irritation.

No corneal damage or irisitis was noted at any time in the rabbit's eyes. However, discharge and redness of the conjunctivae were observed in all animals. Irritation to the conjunctivae appeared to dissipate by 48 hours and was not evident by 72 hours.. The average of the Draize Irritation Scores for 24, 48 and 72 hours was 8, 1 and 0 on a scale of 110 for the six eyes, respectively.

References: [1]Primary Eye Irritation, Monsanto Company, August, 1976.

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[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1g. PRIMARY SKIN IRRITATION STUDY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer CAS # 68002-20-0
Method:	Primary Skin Irritation Study according FHSA
Type:	Primary Skin Irritation
Species/Strain:	Rabbits/New Zealand Albino
Sex:	unknown
Number of animals:	6
Year:	1976
GLP:	no
Results:	Non-irritating
Remark:	This study is assigned a reliability code of 3a according to the criteria established by Klimisch et al. (1997). Documentation insufficient for assessment, therefore this study is not considered valid.

Summary details:

A single 0.5 ml dose of the test article was applied to each an intact and abraded site on each animal. Skin reactions were evaluated ~4, 24, hours and at 2, 3, and 7 days.

At the 24-, 48- and 72-hour evaluations, scores for erythema ranged from 1 to 2 for abraded sites and were none for intact sites. Scores for edema ranged from none for intact sites to a 2 for abraded sites. There were no important differences in skin irritation between intact and abraded sites.

References: [1]Primary Skin Irritation, Monsanto Company, August, 1976.

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[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and

ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

1h. PRIMARY DERMAL IRRITATION STUDY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Follows method described in FIFRA (November, 1982 Section 81-1) and in TSCA: Health Effects Test Guidelines, August 1982.
Type:	Primary Skin Irritation
Species/Strain:	Rabbits/New Zealand Albino
Sex:	4 males/ 2 females
Number of animals:	6
Year:	1988
GLP:	Conducted in the spirit of GLP.
Results:	Mild to Non-irritating
Remark:	This study is assigned a reliability code of 1d according to the criteria established by Klimisch et al. (1997)[2]. Meets generally accepted scientific standards and is described in sufficient detail.

Summary details:

The animal room temperature and relative humidity ranges were 15.5-21.1ºC and 30-70%, respectively. Room temperature and relative humidity were monitored twice daily. Food and water were provided ad libitum. Light was kept on a 12 hours light, 12 hours dark automatically controlled cycle. Animals were randomly selected and subject to a pretest observation prior to dosing. Only healthy animals were chosen for the study.

Animals were checked for viability twice daily and were observed for clinical signs at 30 minutes and at 24, 48, and 72 hours post-patch removal. At each interval all sites were evaluated for erythema and edema or other evidence of dermal irritation according to the Draize[3] scoring system.

The test sites were prepared by closely clipping the hair of each rabbit was closely clipped from the dorsal area of the trunk with an electric clipper, so as to expose at least 10% of the body

surface area.. 24 hours after clipping the hair, a single 0.5 ml dose of the test article as received was applied to a 1-inch square gauze patch and applied to each of the 2 test sites (2 intact) on each animal. The patches were held in place with tape and covered with an occlusive binder. The binder was removed 4 hours later, the test sites were wiped with gauze and acetone to remove remaining test article. Skin reactions were evaluated ~30 minutes after wiping.

The test material produced generally very mild and transient dermal irritation. One of the six animals was free of dermal irritation; five animals exhibited very slight (barely perceptible) erythema without edema at 0.5 hours. Some erythema (very slight or slight) was noted at 24 and/or 48 hours; but all animals were free of dermal irritation within 72 hours after application of the test material.

References: [1]Primary Dermal Irritation Study. Bio/Dynamics for Monsanto Company, Report #4398-87/BD-87-190, January, 1988.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

[3]Draize, J.H., Woodward, G. and Calvery, H.O.: Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Therap. 82: 377-390, 1944.

1i. ACUTE INHALATION TOXICITY[1]

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Whole-Body Inhalation Exposure
Type:	Inhalation LC50
Species/Strain:	Rats/Sprague Dawley
Sex:	Male
Number of animals:	6
Year:	1976
GLP:	no

Results: 6-hour Inhalation LC50 = >0.6 mg/L (highest concentration tested)

Remark: This study is assigned a reliability code of 3a according to the criteria established by Klimisch et al. (1997). Documentation insufficient for assessment, therefore this study is not considered valid.

Summary details:

One group, containing six male rats, was exposed once for 6 hours to an atmosphere generated from the test article. The exposure levels were obtained by adjusting the rate at which the test article was supplied to the generator. The initial sample weighed 116.0 g, the recovered sample was 115.1 g. The nominally calculated vaporized sample was 0.9 g. Temperature (27°C) and relative humidity (80%) in the inhalation chamber was monitored. Airflow was set at 4 L/min. Chamber volume was 35L.

Clinical signs were observed on the day of exposure and during the 14-day recovery period.

None of the animals died during the study. Clinical signs observed in surviving animals during the first day post-exposure consisted of reduced appetite and activity. When removed from the chamber the fur of the animals was a very slight yellow color..

The viscera appeared normal upon gross pathology examination.

References: [1]Acute Inhalation Toxicity, Monsanto Company, August, 1976.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

2. REPEATED DOSE TOXICITY

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	One Month Dermal Study of Resimene® 745 Methylated Melamine-Formaldehyde Resin in Sprague-Dawley Rats.
Type:	28-day Repeated Dose Dermal Toxicity Study
Species/Strain:	Rat/Sprague Dawley
Sex:	males/females
Number of animals:	80
Year:	1990
GLP:	yes
Results:	NOEL = 250 mg/kg/day; No Effect Level = 1000 mg/kg/day
Remark:	This study is assigned a reliability code of 1b according to the criteria established by Klimisch *et al.* (1997)[2]. Comparable to a guideline study, conducted under GLP and is described in sufficient detail.

Summary details:

Dermal applications of methylated melamine-formaldehyde resin (HMMM) were performed at levels of 0, 250, 750 and 1,000 mg/kg/day, five days per week, for approximately four weeks (total exposures were 23 of males and 24 for females) on groups of ten rats of each sex.

All animals survived, and there were no significant changes in body weight, food consumption, clinical observations, hematology, gross and microscopic tissue evaluations. Possibly treatment-related increases in liver and spleen weights in males, and increases in SGOT and SGPT values in females, were noted at either of the two highest doses. However, in the absence of supportive microscopic findings, the biological significance of these changes remains unclear. Based on these results, the dose level of 250 mg/kg/day was considered to be the No-Observable-Effect-Level (NOEL) after one month of exposure for rats. The 1,000 mg/kg/day dose level was considered to be a "no-effect" level.

The test material was applied daily for five days per week to an approximate 25 cm2 shaved area of upper back with a 1cc disposable tuberculin syringe. The exposure site was left unoccluded. A plastic collar was placed on the animals for approximately six hours during exposure to

minimize ingestion. Skin was then wiped clean of remaining test material after each exposure using ethanol. Daily dosages were calculated form each week's body weight data.

Food and water were available ad libitum. Animals were kept on a 12 hours daily light/12 hours dark cycle. Temperature (64.4 to 78.8 F) and relative humidity (40-70%) were monitored with no excursions. Animals were checked twice daily for mortality and morbidity. Detailed observations for signs of toxicity were made once weekly as were body weight and food consumption measurements.

Clinical pathology was performed at study termination on all animals, with food withheld overnight prior to blood collection. Hematology determinations, leukocyte differentials, reticulocyte counts, and blood chemistry was performed on all animals.

Gross pathology was performed on all animals after week 4. External and internal examinations were performed. The brain, heart, kidneys, liver, spleen, and testes with epididymides (paired organs were weighed together) were weighed.

Histopathology was performed on all control and high dose tissues that were retained. This included the major organs plus the reproductive organs (the ovaries, uterus (corpus and cervix) the mammary glands, the prostate, and the testes with epididymides).

Dunnett's Multiple Comparison Test was used to statistically evaluate differences between treated and control animals for body weights, food consumption and reticulocyte counts. Fisher's Exact Test with Bonferroni's Inequality Procedure was used to evaluate the incidence of microscopic lesions. Other statistical tools were used to evaluate the data depending on whether the data were parametric or non-parametric.

Results: There were no deaths during the study. Body weights and food consumption of animals at all dose levels were comparable to controls. There were no clinical signs of dermal irritation or toxicity observed. There were no differences in hematology parameters considered related to treatment. Increases in SGOT (mid and high dose females) and SGPT (high dose females) apparently were related to exposure. Total bilirubin increases in all female exposure groups were attributed to lower than normal control values. Increases in serum globulin and total protein were small in magnitude and did not occur in a dose-related fashion; therefore, they were not considered related to treatment.

Gross and Microscopic Pathology: Increase in absolute and relative liver weights (mid and high dose males) and spleen weights (high dose males) may have been related to treatment. Other organ weight alterations were minor and considered to be of no biological significance. There were no treatment-related gross lesions observed at necropsy. A pair of enlarged adrenal glands (control) and a single incidence of hydrometra (an accumulation of watery fluid in the uterus) in two groups (control and low dose) were noted. No microscopic changes were noted in either the control or high dose groups, and therefore, the intermediate dose groups were not examined.

References: [1]One Month Dermal Study of Resimene® 745 Methylated Melamine-Formaldehyde Resin in Sprague-Dawley Rats.

Monsanto Agricultural Company, Environmental Health Laboratory, Report # MSL-10185, May 30, 1990.

[2]Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

3. DEVELOPMENTAL TOXICITY

Test Substance: Hexamethoxymethylmelamine, CAS # 3089-11-0

No Data Found

4. REPRODUCTIVE TOXICITY

Test Substance: Hexamethoxymethylmelamine, CAS # 3089-11-0

No Data Found

5. GENETIC TOXICITY

a. GENE MUTATIONS

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	Standard Ames Protocol[1]
Type:	Salmonella typhimurium reverse mutation assay
System of testing:	TA-98, TA-100, TA-1535, TA-1537 and TA-1538
Concentrations:	Triplicate cultures of each strain at: 167, 500, 1670, 5000, 7500, & 10,000 μg/plate (100 μL test substance/plate)
Controls:	Positive controls in the absence of S9 = sodium azide (NaN_3) 9-aminoacridine (9-AA) 2-nitrofluorene (2-NF) Positive controls in the presence of S9 = 2-anthramine (2-AA) Negative control = ethanol solvent control
Cytotoxic conc.:	Results of prescreen indicated that Resimene® 745 was not toxic to either TA1538 or TA100 at doses of 50, 167, 500, 1670 and 5000 μg/plate.
Metabolic activation:	with and without Aroclor induced rat liver S-9 (50 μl/plate S-9 preparation)
Year:	1988
GLP:	Yes
Result:	Non-mutagenic
Remark:	This study is assigned a reliability code of 1b according to the criteria established by Klimisch *et al.* (1997)[2]. Comparable to a guideline study, conducted under GLP and is described in sufficient detail.

Summary details:

The test substance was non-mutagenic in the Ames Salmonella Plate Assay with and without metabolic activation (S-9) using bacterial strains TA-98, TA-100, TA-1535, TA-1537, and TA-1538.

Test article was prepared by diluting the test material in ethanol. Desired test concentrations were obtained by serial dilution. A preliminary toxicity screen was performed using TA-100 and TA-1538 to determine the level of toxicity of the test substance. Five doses, in duplicate, were tested for toxicity with a plate assay performed in the manner used for mutagenicity determinations. Toxicity was assessed at 48 hours after treatment by observations for either growth inhibition of the background lawn or a reduction in the number of spontaneous mutants. The maximum concentration tested was 5,000 μg/plate. None of the dose were cytotoxic.

Based on these results, 6 doses ranging from 167 μg/plate to 10,000 μg/plate were selected for the definitive assay. All assays were performed in triplicate cultures in all five tester strains for each test article dose, as well as positive and solvent controls, with and without S9. Treatments were performed by combining 2 ml top agar (supplemented with 0.5 mM histidien/0.5 mM biotin), 0.1 ml tester strain and 0.1 ml test article or solvent in sterile glass tubes preheated to 45ºC. The tubes were vortexed and the mixture was poured onto minimal glucose plates, evenly distributed, and allowed to solidify. Within an hour the plates were inverted and incubated in the dark at 37ºC for 48 hours. Following incubation for 48 hours, the background lawn and spontaneous revertant colonies were enumerated. Inhibited growth was characterized by the absence of a confluent bacterial lawn and /or the presence of pindot colonies.

A positive result is defined as a statistically significant, dose-dependent increase in the number of histidine-independent revertants with at least one dose level inducing a revertant frequency that is two-fold the spontaneous solvent control value. Statistical analyses were performed using the program developed by Snee and Irr (1981)[3] with significance established at the 95% CL. If the test article doses not induce a statistically significant, dose-dependent increase in revertant frequency but dose induce a revertant frequency at one dose level that is two-fold the spontaneous control value, the result is considered equivocal. A negative result is defined as the absence of a statistically significant or dose-dependent increase in the number of histidine-independent revertants.

Normal growth was observed for all strains at all doses with and without S9. Revertant frequencies for all doses in strains TA1535, TA1537, TA98 and TA100 with and without S9, and in strain TA1538 without S9 approximated those observed in the concurrent negative control cultures. Statistically significant increases in revertant frequencies, to approximately 1.6 fold control values were observed in strain TA1538 at doses of 1670 and 10,000 μg/plate. In addition, the increase was apparently dose-dependent. Therefore, the test material was re-evaluated under identical conditions in strain TA1538 at doses of 167, 500, 1670, 5000, 7500 and 10,000 μg/plate with S9. Revertant frequencies for all doses tested in the re-evaluation of strain TA1538 were concurrent with negative control cultures. Thus, the slight increases observed in strain TA1538 with S9 in the original assay are considered to be statistical

aberrations due to random fluctuation of the spontaneous revertant frequency. All positive and negative control values in all assays were within acceptable limits.

The results were negative in the Ames/Salmonella Plate Incorporation Assay under the conditions, and according to the criteria, of the test protocol.

References:

[1]Ames/Salmonella Plate Incorporation Assay PH 301-MO-003-88 (PK-88-402) of Resimene® 745 Lot#8951078 by Pharmakon Research International for Monsanto Company, December 10, 1988.

Ames, B.N., J. McCann, and E. Yamasaki (1975) Methods for detecting carcinogens and mutagens with the Salmonella/Microsome Mutagenicity Test, Mutation Res., 31:347-364.

Maron D.M., J. Katzenellenbogen and B.N. Ames (1981) Compatibility of organic solvents with the Salmonella/Microsome Test, Mutation Res., 88:343-350

Maron, D.M. and B.N. Ames (1983) Revised methods for the Salmonella mutagenicity test, Mutation Res., 113:173-215.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

[3]Snee, R.D. and J.D. Irr (1981). Design of statistical method for the analysis of mutagenesis at the hypoxanthine guanine phosphoribosyl transferase locus of cultured Chinese hamster ovary cells, Mutation Res., 85:77-93.

b. CHROMOSOMAL ABERRATIONS (In Vitro)

Test Substance: ~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS# 68002-20-0

Method: In Vitro Chromosome Aberration Analysis In Chinese Hamster Ovary (CHO) Cells[1]

Type:	In Vitro Chromosome Aberration Analysis
System of testing:	CHO-K1-BH4 Cells, Lot #A-12. This is a continuous cell line with the modal number of 20 chromosomes with a population doubling time of 12-14 hours.
Concentrations:	The test material was dissolved in 95% ethanol. Doses tested were 87.5, 350 and 900 μg/ml without S9 and 292, 1000 and 2500 μg/ml with S9.
Cytotoxic conc.:	1000 to 5000 μg/ml without S9 and 5000 μg/ml with S9.
Controls:	Positive control in the absence of S9 = N-methyl-N-nitro-N-nitrosoguanidine (MNNG) dissolved in ethanol for a treatment concentration of 2.0 μg/ml of medium. Positive control in the presence of S9 = N-Nitrosodimethylamine (DMN) dissolved in distilled water for a treatment concentrations of 1000 μg/ml of medium. Negative control = 95% ethanol solvent control with and without metabolic activation.
Metabolic activation:	with and without Aroclor induced rat liver S-9
Year:	1989
GLP:	Yes
Result:	HMMM was determined to be positive in its ability to produce chromosome aberrations in CHO cells under the experimental conditions of this laboratory.
Remark:	This study is assigned a reliability code of 1b according to the criteria established by Klimisch *et al.* (1997)[2]. Comparable to a guideline study, conducted under GLP and is described in sufficient detail.

Summary details:

Cytotoxicity: Single cultures of CHO-K1-BH4 cells were prepared at a density of 6 $x10^5$ cells/80 cm^2 flask in F12FCM(5%) medium containing 5% heat-inactivated fetal bovine serum (FBS). Following the growth period, the medium was aspirated from each flask, the cultures

were washed and fresh medium was added. Non-activated cultures were supplied with 10 ml medium and activated cultures with 8 ml medium and 2 ml of S9 mixture. Treatment was initiated by the addition of 100 µl of test article or control dilutions to the appropriate cultures. Cultures were incubated for five hours. After treatment, culture were washed three times then medium and BrdUrd were dispensed to each flask. Flasks were incubated for an additional 27 hours. For the last 2-3 hours of incubation, colcemid was added to each culture to arrest cells in metaphase. At the end of incubation, cell suspensions were collected by trypsinization and slides were prepared and stained for sister chromatid differentiation.

Aberration Assay: Duplicate cultures of CHO-K1-BH4 cells were prepared at a density of 8 x 105cells/980 cm2 flask in 15 ml medium containing 5% FBS. Cultures were established for each control and treatment dose level both with and without S9. Cells were allowed to grow for ~16-24 hours. Following the growth period, the medium was aspirated from each flask, the cultures were washed and fresh medium was added. Non-activated cultures were supplied with 10 ml medium and activated cultures with 8 ml medium and 2 ml of S9 mixture. Treatment was initiated by the addition of 100 µl of test article or control dilutions to the appropriate cultures. Cultures were incubated for 5 hours.

Following treatment, cells were washed three times and then fresh medium was added. The cultures were incubated an additional 18 hours, for the last 2-3 hours, colcemid was added to each culture to arrest cells in metaphase.

At the end of incubation, cells suspensions were collected by the mitotic shake-off method. Cells were sedimented by centrifugation and hypotonic KCl was added to swell the cells. Cells were fixed with three washes of methanol:glacial acetic acid (3:1) and slides prepared by standard methods.

A total of 100 metaphases were scored for the presence of chromosome aberration per data point. Fifty (50) metaphases were obtained per culture and data pooled for analysis. Cytogenetic abnormalities were classified on a standard scoring sheet according to chromosome or chromatid aberrations and further according to type of aberrations. Aberrations were classified according to the nomenclature of Buckton and Evans, 1973 and Savage, 1975.

Data were evaluated by using the Chi-Square analysis of the aberrant cells versus the normal cells comparing each group to its concurrent solvent control.

Results indicated the test material induced a statistically significant increase in aberrations/cell and proportion of aberrant metaphases at 900 µg/ml without S9 and at 1000 and 2500 µg/ml with S9. In addition, the results with S9 mix produced a dose-related increase in aberrations/cell and proportion of aberrant metaphases. Therefore, the test material is more clastogenic with exogenous metabolic activation than without.

References

[1]In Vitro Chromosome Aberration Analysis In Chinese Hamster Ovary (CHO) Cells PH 320-MO-004-88 (PK-88-403) of Resimene® 745 by Pharmakon Research International for Monsanto Company, February 15, 1989.

Buckton, K.E. and H.J. Evans, Methods for the Analysis of Human Chromosome Aberrations. World Health Organization, Geneva 1973.

EPA New and Revised Health Effects Guidelines, Office of Pesticides and Toxic Substances, Report No. EPA 560/6-82-001, 1983. Environmental Protection Agency Federal Register Vol. 50, No. 188, Friday, September 27, 1985.

Preston, J. et al., 1981. In vivo and In vitro cytogenetic assays: A report of the U.S. EPA "gene-Tox" Program. Mutation Res., 87, 143-188.

Savage, J.R.K., 1975. Classification and Relationships of Induced Chromosomal Structural Changes. Journal of Med. Genetics 12:103-122.

Terasima, T. and Tolmach, L.J., 1961. Changes in X-ray sensitivity of HeLa cells during the division cycle. Nature 190:1210-1211.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

c. CHROMOSOMAL ABERRATIONS (In Vivo)

Test Substance:	~29±1% Hexamethoxymethylmelamine, CAS # 3089-11-0; ~71% Methylated melamine-formaldehyde polymer, CAS # 68002-20-0
Method:	In Vivo Bone Marrow Cytogenetics Rat Metaphase Analysis[1]
Type:	In Vivo Chromosome Aberration Analysis
System of testing:	Sprague Dawley Rat (5 males and 5 females per group)
Concentrations:	Preliminary Dose-Range Finding Study: 500 – 3250 mg/kg.
	Main Study: 170, 935, and 1700 mg/kg. Due to the mortality observed in the three highest concentrations of the range finder and

	the moderate pharmacotoxic signs observed in the next lower dose group (1500 mg/kg), 1700 mg/kg was selected as the highest dose as an estimate of the maximum tolerated dose.
Controls:	Positive control = Cyclophosphamide at 20 mg/kg Negative control = Corn oil
Year:	1989
GLP:	Yes
Result:	1700 mg/kg did not produce significant increases in the number of aberrations or in the number of aberrant metaphase at any of the three sacrifice times evaluated. The test material was judged to be negative in its ability to induce structural chromosomal aberrations to the hemopoietic cells of the rat bone marrow under the experimental conditions of this assay.
Remark:	This study is assigned a reliability code of 1b according to the criteria established by Klimisch *et al.* (1997)[2]. Comparable to a guideline study, conducted under GLP and is described in sufficient detail.

Summary details:

The test substance was administered at 1700 mg/kg and the vehicle control (corn oil) were administered in a single oral dose to six groups of male rats and bone marrow cells were harvested at 6, 18 and 30 hours post-dose. Three extra groups of rats were also dosed, one group dosed with the positive control, cyclophosphamide and the other two groups with the test material at 170 and 935 mg/kg. The three groups were sacrificed 18 hours later. Approximately two hours prior to each scheduled termination, animals were administered colchicine at 4 mg/kg bw to arrest cells in metaphase. At the appropriate time, animals were sacrificed and both femurs were removed from each animals and metaphase slides prepared. Slides were stained, coded and scored for chromosomal aberrations.

Two rats dosed with 1700 mg/kg died and a few more exhibited severe pharmacotoxic signs. These observations suggest that the test material was evaluated at or near the maximum tolerated dose.

A total of 50 metaphase cells were analyzed for each animal for the presence of chromatid and chromosome type aberrations. Aberrations were classified according to type on a standard scoring sheet and the number of aberrations in each cell tabulated. The number of centromeres in each cell was counted and recorded.

Data were evaluated for statistically significant increases in aberrations per cell in treatment groups as compared to the respective negative control group. The proportion of aberrant

metaphases was also evaluated for statistically significant increases over the negative control groups. Data were evaluated separately for each harvest time.

The positive control article, cyclophosphamide, resulted in significant increases in the incidence of chromosome aberrations and in the proportion of metaphases with one or more aberrations.

No statistically significant increase in the incidence of aberrations or in the number of cells with one or more aberrations were observed in animal treated at a dose of 1700 mg/kg at any of the three sampling times evaluated.

References

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Savage, J.R.K., 1975. Classification and Relationships of Induced Chromosomal Structural Changes. Journal of Med. Genetics 12:103-122.

[2] Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997. See Listing of Codes, p. 52.

J. GENERAL REFERENCE

Klimisch, H.J., Andreae, M and Tillman, U. A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*. 25: 1-5, 1997.

1 = Valid without restriction

1a: GLP guideline study
1b: Comparable to guideline study
1c: Meets national standard methods (AFNOR/DIN)
1d: Meets generally accepted scientific standards and is described in sufficient detail

2 = Valid with restriction

2a: Guideline study without detailed documentation
2b: Guideline study with acceptable restrictions
2c: Comparable to guideline study with acceptable restrictions
2d: Meets national standard methods with acceptable restrictions
2e: Meets generally accepted scientific standards, well-documented and acceptable for assessment
2f: Accepted calculation method
2g: Data from Handbook or collection of data

3 = Invalid

3a: Documentation insufficient for assessment
3b: Significant methodological deficiencies
3c: Unsuitable test system

4 = Not assignable

4a: Abstract
4b: Secondary literature
4c: Original reference not yet available
4d: Original reference in foreign language
4e: Documentation insufficient for assessment.